Please amend the application as follows:

In the Claims

Please cancel Claim 24.

Please amend Claims 1, 2, 8, 10, 11, 15, 16, 21, 22, 25 and 26. Amendments to the claims are indicated in the attached "Marked Up Version of Amendments" (pages i - iii).

1. (Amended) A method of altering the acetylation status of at least one amino acid residue in a protein, the acetylation status consisting essentially of an NAD-dependent acetylation status comprising the step of altering the activity of a Sir2 protein.

2. (Amended) The method of Claim 1, wherein the protein is a histone protein.

8. (Amended) The method according to Claim 7, wherein the Sir2α protein has an amino acid sequence selected from the group consisting of SEQ ID NOS: 1, 4, 9, 12, 19 and 26.

10. (Amended) The method of Claim 7, wherein the Sir2α protein is a mutant Sir2α protein selected from the group consisting of G253A, G255A, S257A, I262A, F265A, R266A, G270A, P285A, T336A, H355A, Thr-261, Iso-271, Arg-275 and Asn-345.

11. (Amended) A method of identifying an agent which alters the activity of a Sir2 protein by assessing the ability of the agent to alter the acetylation status of at least one amino acid in a protein, the acetylation status consisting essentially of an NAD-dependent acetylation status, comprising the steps of:

a) combining the protein, the Sir2 protein, NAD or an NAD-like compound and the agent to be tested, thereby producing a combination;

b) detecting the NAD-dependent acetylation status of an amino acid in the protein in the combination; and

c) comparing the NAD-dependent acetylation status of an amino acid in the protein in the combination with the NAD-dependent acetylation status of the amino acid in the protein in the absence of the agent to be tested,

wherein a difference in the NAD-dependent acetylation status of the amino acid of the protein in the presence of the agent as compared with the absence of the agent indicates that the agent alters the NAD-dependent acetylation status of at least one amino acid of the protein.

15. (Amended) The method of Claim 63, wherein the histone protein is selected from the group consisting of an H2B, H3 and H4 histone protein.

16. (Amended) The method of Claim 63, wherein the NAD-dependent acetylation in the histone protein is acetylation of a lysine amino acid residue.

21. (Amended) A method of identifying an agent which alters life span of a cell by assessing the ability of the agent to alter the acetylation status of at least one amino acid in a protein, the acetylation status consisting essentially of an NAD-dependent acetylation status, comprising the steps of:

a) combining the protein, a Sir2 protein, NAD or an NAD-like compound and the agent to be tested, thereby producing a combination;

b) detecting the NAD-dependent acetylation status of an amino acid in the protein in the combination; and

c) comparing the NAD-dependent acetylation status of an amino acid in the protein in the combination with the acetylation status of the amino acid in the protein in the absence of the agent to be tested,

wherein a difference in the acetylation status of the amino acid of the protein in the presence of the agent as compared with the acetylation status of the amino acid of the histone protein in the absence of the agent indicates that the agent alters the life span of the cell.

22. (Amended) The method of Claim 64, wherein the histone protein is selected from the group consisting of an H2B, H3 and H4 histone protein.

25. (Amended) A method of altering the acetylation status of at least one amino acid residue in a protein, the acetylation status consisting essentially of an NAD-dependent acetylation status, comprising the step of combining the protein, a Sir2 protein and NAD or an NAD-like compound.

26. (Amended) The method of Claim 25, wherein the protein is a histone protein.

Please add new Claims 62-67.

62. (New) The method of Claim 2, wherein the histone protein is selected from the group consisting of an H2B, H3 and H4 histone protein.

63. (New) The method of Claim 11, wherein the protein is a histone protein.

64. (New) The method of Claim 21, wherein the protein is a histone protein.

65. (New) The method of Claim 26, wherein the histone protein is selected from the group consisting of an H2B, H3 and H4 histone protein.

66. (New) A method of altering the life span of a cell, comprising the step of administering to the cell an agent which alters the acetylation status of at least one amino acid in a protein, the acetylation status consisting essentially of an NAD-dependent acetylation status, by altering the activity of a Sir2 protein, wherein the agent is identified by a method, comprising the steps of:

a) combining the protein, a Sir2 protein, NAD or an NAD-like compound and the agent to be tested, thereby producing a combination;

b) detecting the NAD-dependent acetylation status of an amino acid in the protein in the combination; and

c) comparing the NAD-dependent acetylation status of an amino acid in the protein in the combination with the acetylation status of the amino acid in the protein in the absence of the agent to be tested,

wherein a difference in the acetylation status of the amino acid of the protein in the presence of the agent as compared with the acetylation status of the amino acid of the histone protein in the absence of the agent indicates that the agent alters the life span of the cell.

67. (New) The method of Claim 26, wherein the protein is a histone protein.

REMARKS

The remainder of this Reply is set forth under appropriate sub-headings for the convenience of the Examiner.

Claim Amendments

Claim 1 has been amended to include the phrase "comprising the step of" in the preamble. Claim 25 has been amended to include the phrase "the step" in the method.

Claims 8, 10, 15 and 22 have been amended to include the proper alternative expression "and" for the Markush group in the claims.

Claims 15, 16 and 22 have been amended to correct their dependency, in light of new Claims 63 and 64.

Claims 11, 21 and 25 have been amended to eliminate the limitation that the protein is a histone protein and to include the limitation that the acetylation status that is altered by the method of the invention consists essentially of NAD-dependent acetylation status. Support for the amendment to eliminate the limitation that the protein is a histone protein can be found in the specification, for example, at page 2, line 7-9; and page 15, line 24 through page 16, line 2.